OIPE

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/600,991 DATE: 09/07/2001 TIME: 14:13:11

Input Set : A:\0471-0162P.ST25.txt

Output Set: N:\CRF3\09072001\I600991.raw

| | 3 | <110> APPL | CANT: MEDIC | CO, Enzo | | | | | | | | | |
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| | 4 | MICH | IELI, Paolo | | | | | | | | | | |
| | 5 | COLLESI, Chiara | | | | | | | | | | | |
| | 6 | CASELLI, Gianfranco | | | | | | | | | | | |
| | 7 | COMO | GLIO, Paolo | | 젊 | | | | | | | | |
| | 9 | <120> TITLE | OF INVENT | ON: RECOMB | INANT PROTE | INS DERIVED | FROM HGF AN | | | | | | |
| | 11 | <130> FILE | REFERENCE: | 0471-0162P | | | | <u> </u> | - | | | | |
| | 13 | <140> CURRI | ENT APPLICAT | | | <u> </u> | | | | | | | |
| C> | 14 | <141> CURRI | ENT FILING I | | | | P | | | | | | |
| | 16 | <160> NUMBI | ER OF SEQ II | | | | | | | | | | |
| | 18 | <170> SOFTW | WARE: Patent | | | | | | | | | | |
| | 20 | <210> SEQ 3 | ID NO: 1 | | 600/2900 | 2001 | | | | | | | |
| | 21 | <211> LENGT | rH: 1725 | | | | | 8 | 01 | | | | |
| | 22 | <212> TYPE | : DNA | | | | • | . 199 | | | | | |
| | 23 | <213> ORGAN | NISM: Artifi | | | 8 | | | | | | | |
| | 25 | <220> FEATU | JRE: | | | | | | | | | | |
| | 26 | <223> OTHER | R INFORMATIO | | | | | | | | | | |
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| | 29 | atgtgggtga | ccaaactcct | gccagccctg | ctgctgcagc | atgtcctcct | gcatctcctc | 60 | | | | | |
| | 30 | ctgctcccca | tcgccatccc | ctatgcagag | ggacaaagga | aaagaagaaa | tacaattcat | 120 | | | | | |
| | 31 | gaattcaaaa | aatcagcaaa | gactacccta | atcaaaatag | atccagcact | gaagataaaa | 180 | | | | | |
| | 32 | accaaaaaag | tgaatactgc | agaccaatgt | gctaatagat | gtactaggaa | taaaggactt | 240 | | | | | |
| | 33 | ccattcactt | gcaaggcttt | tgtttttgat | aaagcaagaa | aacaatgcct | ctggttcccc | 300 | | | | | |
| | 34 | ttcaatagca | tgtcaagtgg | agtgaaaaaa | gaatttggcc | atgaatttga | cctctatgaa | 360 | | | | | |
| | 35 | aacaaagact | acattagaaa | ctgcatcatt | ggtaaaggac | gcagctacaa | gggaacagta | 420 | | | | | |
| | 36 | tctatcacta | agagtggcat | caaatgtcag | ccctggagtt | ccatgatacc | acacgaacac | 480 | | | | | |
| | 37 | agctatcggg | gtaaagacct | acaggaaaac | tactgtcgaa | atcctcgagg | ggaagaaggg | 540 | | | | | |
| | 38 | ggaccctggt | gtttcacaag | caatccagag | gtacgctacg | aagtctgtga | cattcctcag | 600 | | | | | |
| | 39 | tgttcagaag | ttgaatgcat | gacctgcaat | ggggagagtt | atcgaggtct | catggatcat | 660 | | | | | |
| | 40 | acagaatcag | gcaagatttg | tcagcgctgg | gatcatcaga | caccacaccg | gcacaaattc | 720 | | | | | |
| | 41 | ttgcctgaaa | gatatcccga | caagggcttt | gatgataatt | attgccgcaa | tcccgatggc | 780 | | | | | |
| | 42 | cagccgaggc | catggtgcta | tactcttgac | cctcacaccc | gctgggagta | ctgtgcaatt | 840 | | | | | |
| | 43 | aaaacatgcg | ctgacaaagc | ttcgggcggt | ggcggttctg | gtggcggtgg | ctccggcggt | 900 | | | | | |
| | 44 | ggcggttctc | tagagggaca | aaggaaaaga | agaaatacaa | ttcatgaatt | caaaaaatca | 960 | | | | | |
| | 45 | gcaaagacta | ccctaatcaa | aatagatcca | gcactgaaga | taaaaaccaa | aaaagtgaat | 1020 | | | | | |
| | 46 | actgcagacc | aatgtgctaa | tagatgtact | aggaataaag | gacttccatt | cacttgcaag | 1080 | | | | | |
| | 47 | gcttttgttt | ttgataaagc | aagaaaacaa | tgcctctggt | tccccttcaa | tagcatgtca | 1140 | | | | | |
| | 48 | agtggagtga [·] | aaaaagaatt | tggccatgaa | tttgacctct | atgaaaacaa | agactacatt | 1200 | | | | | |
| | 49 | agaaactgca | tcattggtaa | aggacgcagc | tacaagggaa | cagtatctat | cactaagagt | 1260 | | | | | |
| | 50 | ggcatcaaat | gtcagccctg | gagttccatg | ataccacacg | aacacagcta | tcggggtaaa | 1320 | | | | | |
| | 51 | gacctacagg | aaaactactg | tcgaaatcct | cgaggggaag | aagggggacc | ctggtgtttc | 1380 | | | | | |
| | 52 | acaagcaatc | cagaggtacg | ctacgaagtc | tgtgacattc | ctcagtgttc | agaagttgaa | 1440 | | | | | |
| | 53 | tgcatgacct | gcaatgggga | gagttatcga | ggtctcatgg | atcatạcaga | atcaggcaag | 1500 | | | | | |
| | 54 | atttgtcagc | gctgggatca | tcagacacca | caccggcaca | aattcttgcc | tgaaagatat | 1560 | | | | | |
| | 55 | cccgacaagg | gctttgatga | taattattgc | cgcaatcccg | atggccagcc | gaggccatgg | 1620 | | | | | |
| | 56 | tgctatactc | ttgaccctca | cacccgctgg | gagtactgtg | caattaaaac | atgcgctgac | 1680 | | | | | |
| | 57 | aaagctgacg | acgacgacaa | acaccaccac | caccaccacc | actag | | 1725 | | | | | |
| | | | | | | | | | | | | | |

RAW SEQUENCE LISTING DATE: 09/07/2001 PATENT APPLICATION: US/09/600,991 TIME: 14:13:11

Input Set.: A:\0471-0162P.ST25.txt

Output Set: N:\CRF3\09072001\I600991.raw

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    66 <223> OTHER INFORMATION: Magic F-1 recombinant protein obtained combining hairpin loop
and
    67
             kringle domains of human HGF and MSP
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                                            10
                                                                15
    74 Leu His Leu Leu Leu Pro Ile Ala Ile Pro Tyr Ala Glu Gly Gln
    75
                    20
                                        25
                                                            30
    77 Arg Lys Arg Arg Asn Thr Ile His Glu Phe Lys Lys Ser Ala Lys Thr
    78
                                    40
    80 Thr Leu Ile Lys Ile Asp Pro Ala Leu Lys Ile Lys Thr Lys Lys Val
    81
            50
                                55
                                                    60
    83 Asn Thr Ala Asp Gln Cys Ala Asn Arg Cys Thr Arg Asn Lys Gly Leu
    84 65
                            70
                                                                    80
    86 Pro Phe Thr Cys Lys Ala Phe Val Phe Asp Lys Ala Arg Lys Gln Cys
    87
                       85
                                            90
                                                                95
    89 Leu Trp Phe Pro Phe Asn Ser Met Ser Ser Gly Val Lys Lys Glu Phe
                   100
    90
                                        105
                                                            110
    92 Gly His Glu Phe Asp Leu Tyr Glu Asn Lys Asp Tyr Ile Arg Asn Cys
    93
               115
                                   120
                                                        125
    95 Ile Ile Gly Lys Gly Arg Ser Tyr Lys Gly Thr Val Ser Ile Thr Lys
    96
           130
                                135
                                                    140
    98 Ser Gly Ile Lys Cys Gln Pro Trp Ser Ser Met Ile Pro His Glu His
                            150
                                                155
                                                                    160
    99 145
    101 Ser Tyr Arg Gly Lys Asp Leu Gln Glu Asn Tyr Cys Arg Asn Pro Arg
                                             170
    102
                        165
    104 Gly Glu Glu Gly Pro Trp Cys Phe Thr Ser Asn Pro Glu Val Arg
    105 180 185
    107 Tyr Glu Val Cys Asp Ile Pro Gln Cys Ser Glu Val Glu Cys Met Thr
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                195
    110 Cys Asn Gly Glu Ser Tyr Arg Gly Leu Met Asp His Thr Glu Ser Gly
                                 215
                                                     220
    111
             210
    113 Lys Ile Cys Gln Arg Trp Asp His Gln Thr Pro His Arg His Lys Phe
                                                 235
    114 225
                             230
                                                                     240
    116 Leu Pro Glu Arg Tyr Pro Asp Lys Gly Phe Asp Asp Asn Tyr Cys Arg
    117
                         245
                                             250
    119 Asn Pro Asp Gly Gln Pro Arg Pro Trp Cys Tyr Thr Leu Asp Pro His
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122 Thr Arg Trp Glu Tyr Cys Ala Ile Lys Thr Cys Ala Asp Lys Ala Ser

125 Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Leu

128 Glu Gly Gln Arg Lys Arg Arg Asn Thr Ile His Glu Phe Lys Lys Ser

131 Ala Lys Thr Thr Leu Ile Lys Ile Asp Pro Ala Leu Lys Ile Lys Thr

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PATENT APPLICATION: US/09/600,991 TIME: 14:13:11

Input Set : A:\0471-0162P.ST25.txt
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134 Lys Lys Val Asn Thr Ala Asp Gln Cys Ala Asn Arg Cys Thr Arg Asn 137 Lys Gly Leu Pro Phe Thr Cys Lys Ala Phe Val Phe Asp Lys Ala Arg 140 Lys Gln Cys Leu Trp Phe Pro Phe Asn Ser Met Ser Ser Gly Val Lys 143 Lys Glu Phe Gly His Glu Phe Asp Leu Tyr Glu Asn Lys Asp Tyr Ile 390 -146 Arg Asn Cys Ile Ile Gly Lys Gly Arg Ser Tyr Lys Gly Thr Val Ser 149 Ile Thr Lys Ser Gly Ile Lys Cys Gln Pro Trp Ser Ser Met Ile Pro 152 His Glu His Ser Tyr Arg Gly Lys Asp Leu Gln Glu Asn Tyr Cys Arg 155 Asn Pro Arg Gly Glu Glu Gly Gly Pro Trp Cys Phe Thr Ser Asn Pro 158 Glu Val Arg Tyr Glu Val Cys Asp Ile Pro Gln Cys Ser Glu Val Glu 159 465 161 Cys Met Thr Cys Asn Gly Glu Ser Tyr Arg Gly Leu Met Asp His Thr 164 Glu Ser Gly Lys Ile Cys Gln Arg Trp Asp His Gln Thr Pro His Arg 167 His Lys Phe Leu Pro Glu Arg Tyr Pro Asp Lys Gly Phe Asp Asp Asn 170 Tyr Cys Arg Asn Pro Asp Gly Gln Pro Arg Pro Trp Cys Tyr Thr Leu 173 Asp Pro His Thr Arg Trp Glu Tyr Cys Ala Ile Lys Thr Cys Ala Asp 174 545 176 Lys Ala Asp Asp Asp Asp Lys His His His His His His 180 <210> SEQ ID NO: 3 181 <211> LENGTH: 1692 182 <212> TYPE: DNA 183 <213> ORGANISM: Artificial Sequence 185 <220> FEATURE: 186 <223> OTHER INFORMATION: Metron F-1 DNA coding sequence 188 <400> SEQUENCE: 3 189 atggggtggc tcccactcct gctgcttctg actcaatgct taggggtccc tgggcagcgc 190 tcgccattga atgacttcca agtgctccgg ggcacagagc tacagcacct gctacatgcg 191 gtggtgcccg ggccttggca ggaggatgtg gcagatgctg aagagtgtgc tggtcgctgt 192 gggcccttaa tggactgccg ggccttccac tacaacgtga gcagccatgg ttgccaactg 193 ctgccatgga ctcaacactc gccccacacg aggctgcggc gttctgggcg ctgtgacctc 194 ttccagaaga aagactacgt acggacctgc atcatgaaca atggggttgg gtaccggggc 195 accatggcca cgaccgtggg tggcctgccc tgccaggctt ggagccacaa gttcccgaat 196 gatcacaagt acacgcccac tctccggaat ggcctggaag agaacttctg ccgtaaccct

197 gatggcgacc ccggaggtcc ttggtgctac acaacagacc ctgctgtgcg cttccagagc

198 tgcggcatca aatcctgccg ggaggccgcg tgtgtctggt gcaatggcga ggaataccgc

199 ggcgcggtag accgcacgga gtcagggcgc gagtgccagc gctgggatct tcagcacccg

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Input Set : A:\0471-0162P.ST25.txt

Output Set: N:\CRF3\09072001\1600991.raw

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                                                                               900
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                                                                              1080
     207 ctctggttcc ccttcaatag catgtcaagt ggagtgaaaa aagaatttgg ccatgaattt
                                                                              1140
                                                                              1200
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                                                                              1260
     209 aagggaacag tatctatcac taagagtggc atcaaatgtc agccctggag ttccatgata
     210 ccacacgaac acagctatcg gggtaaagac ctacaggaaa actactgtcg aaatcctcga
                                                                              1320
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                                                                              1380
     212 gacattcctc agtgttcaga agttgaatgc atgacctgca atggggagag ttatcgaggt
                                                                              1440
     213 ctcatggatc atacagaatc aggcaagatt tgtcagcgct gggatcatca gacaccacac
                                                                              1500
     214 cggcacaaat tcttgcctga aagatatccc gacaagggct ttgatgataa ttattgccgc
                                                                              1560
                                                                              1620
     215 aatcccgatg gccagccgag gccatggtgc tatactcttg accctcacac ccgctgggag
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                                                                              1692
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     221 <211> LENGTH: 563
     222 <212> TYPE: PRT
     223 <213> ORGANISM: Artificial Sequence
     225 <220> FEATURE:
     226 <223> OTHER INFORMATION: Metron F-1 recombinant protein obtained combining hairpin
loop and
               kringle domains of human HGF and MSP
     227
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                                         25
                     20
     237 Glu Leu Gln His Leu Leu His Ala Val Val Pro Gly Pro Trp Gln Glu
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                                     40
     238
     240 Asp Val Ala Asp Ala Glu Glu Cys Ala Gly Arg Cys Gly Pro Leu Met
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     243 Asp Cys Arg Ala Phe His Tyr Asn Val Ser Ser His Gly Cys Gln Leu
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     246 Leu Pro Trp Thr Gln His Ser Pro His Thr Arg Leu Arg Arg Ser Gly
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                     100
     252 Asn Asn Gly Val Gly Tyr Arg Gly Thr Met Ala Thr Thr Val Gly Gly
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                                     120
     253
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     255 Leu Pro Cys Gln Ala Trp Ser His Lys Phe Pro Asn Asp His Lys Tyr
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                                 135
                                                      140
     258 Thr Pro Thr Leu Arg Asn Gly Leu Glu Glu Asn Phe Cys Arg Asn Pro
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                                                                      160
                             150
                                                  155
     261 Asp Gly Asp Pro Gly Gly Pro Trp Cys Tyr Thr Thr Asp Pro Ala Val
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     264 Arg Phe Gln Ser Cys Gly Ile Lys Ser Cys Arg Glu Ala Ala Cys Val
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RAW SEQUENCE LISTING DATE: 09/07/2001 PATENT APPLICATION: US/09/600,991 TIME: 14:13:11

Input Set : A:\0471-0162P.ST25.txt

Output Set: N:\CRF3\09072001\I600991.raw

| 265 | | | | 100 | | | | | 1 Ó F | | | | | 100 | | |
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| 265 | | ~ | | 180 | a 1 | a 1 | _ | _ | 185 | | | _ | | 190 | - 3 | _ |
| | Trp | Cys | | GLY | GLu | GIu | Tyr | _ | GIY | Ala | Val | Asp | _ | Thr | GLu | Ser |
| 268 | ~ 1 | • | 195 | ~ | a 1 | _ | _ | 200 | _ | ~ 1 | | _ | 205 | ~ 1 | | _ |
| | GLY | _ | Glu | Cys | GIn | Arg | _ | Asp | Leu | GIn | Hls | | His | Gln | Hls | Pro |
| 271 | -1 | 210 | _ | ~ 1 | _ | ' | 215 | _ | | | _ | 220 | _ | _ | _ | _ |
| | | Glu | Pro | GLY | Lys | | Leu | Asp | GIn | GLY | | Asp | Asp | Asn | Tyr | _ |
| | 225 | | _ | _ | | 230 | | _ | _ | _ | 235 | _ | | - | _ | 240 |
| | Arg | Asn | Pro | Asp | _ | Ser | Glu | Arg | Pro | _ | Cys | Tyr | Thr | Thr | _ | Pro |
| 277 | | | | | 245 | | | | | 250 | | | | | 255 | |
| | Gln | Ile | Glu | _ | Glu | Phe | Cys | Asp | | Pro | Arg | Cys | Gly | Ser | Glu | Ala |
| 280 | | | | 260 | _ | | | | 265 | | | | | 270 | | |
| | Gln | Pro | Arg | Leu | Glu | Gly | Gly | _ | Gly | Ser | Gly | Gly | Gly | Gly | Ser | Gly |
| 283 | | | 275 | | | | | 280 | | | | | 285 | | | |
| 285 | Gly | Gly | Gly | Ser | Leu | Glu | Gly | Gln | Arg | Lys | Arg | Arg | Asn | Thr | Ile | His |
| 286 | | 290 | | | | | 295 | | | | | 300 | | | | |
| 288 | Glu | Phe | Lys | Lys | Ser | Ala | Lys | Thr | Thr | Leu | Ile | Lys | Ile | Asp | Pro | Ala |
| 289 | 305 | | | | | 310 | | | | | 315 | | | | | 320 |
| 291 | Leu | Lys | Ile | Lys | Thr | Lys | Lys | Val | Asn | Thr | Ala | Asp | Gln | Cys | Ala | Asn |
| 292 | | | | | 325 | | | | | 330 | | | | | 335 | |
| 294 | Arg | Cys | Thr | Arg | Asn | Lys | Gly | Leu | Pro | Phe | Thr | Cys | Lys | Ala | Phe | Val |
| 295 | | | | 340 | | | | | 345 | | | | | 350 | | |
| 297 | Phe | Asp | Lys | Ala | Arg | Lys | Gln | Cys | Leu | Trp | Phe | Pro | Phe | Asn | Ser | Met |
| 298 | | | 355 | | | | | 360 | | | | | 365 | | | |
| 300 | Ser | Ser | Gly | Val | Lys | Lys | Glu | Phe | Gly | His | Glu | Phe | Asp | Leu | Tyr | Glu |
| 301 | | 370 | _ | | _ | _ | 375 | | _ | | | 380 | - | | _ | |
| | Asn | Lys | Asp | Tyr | Ile | Arq | Asn | Cys | Ile | Ile | Gly | Lys | Gly | Arg | Ser | Tyr |
| | 385 | _ | _ | • | | 390 | | • | | | 395 | • | - | , | | 400 |
| | | Glv | Thr | Val | Ser | Ile | Thr | Lvs | Ser | Glv | Ile | Lys | Cvs | Gln | Pro | Trp |
| 307 | - <u>-</u> - | 2 | | | 405 | | | 4 | | 410 | | • | 1 | | 415 | - |
| | Ser | Ser | Met | Ile | | His | Glu | His | Ser | | Arg | Glv | Lvs | Asp | | Gln |
| 310 | | | | 420 | | | | | 425 | - 1 | , | | 4 | 430 | | |
| | Glu | Asn | Tvr | | Ara | Asn | Pro | Ara | | Glu | Glu | Glv | Glv | Pro | Trp | Cvs |
| 313 | | | 435 | - 1 - | ر | | | 440 | 1 | | | 1 | 445 | | | - 4 - |
| | Phe | Thr | | Asn | Pro | Glu | Val | | Tvr | Glu | Val | Cvs | Asp | Ile | Pro | Gln |
| 316 | | 450 | | | | | 455 | 5 | -1- | | | 460 | | | | |
| | Cvs | | Glu | Val | Glu | Cvs | | Thr | Cvs | Asn | Glv | | Ser | Tyr | Ara | Glv |
| | 465 | 001 | Olu | val | OIU | 470 | | ~ * * * * | O ₁ D | 11011 | 475 | 014 | 501 | -] - | ••• | 480 |
| | | Met | Δen | Hic | Thr | | Ser | Glv | T.vs | Tle | | Gln | Δrα | Trp | Asn | |
| 322 | пса | ricc | пор | 1112 | 485 | Giu | JCI | GIY | · | 490 | Cys | 0111 | nr 9 | 111 | 495 | 1113 |
| | Cln | Пhт | Dro | цiс | | ыiс | Tvc | Dho | Τού | | Glu | λκα | Пτεν | Pro | | Luc |
| 325 | GIII | TIIT | PIO | 500 | Arg | III | цγ | rne | 505 | 110 | Giu | Arg | тут | 510 | кэр | цуз |
| | C1 | Dho | 7 00 | | A a n | Пттъ | Crro | 7 × ~ | | Dro | n an | C1** | Cln | | 7 ~~ | Dro |
| | СТА | Pile | - | ASP | ASII | тАт | Cys | _ | ASII | PIO | ASP | GIY | | Pro | ALG | PIO |
| 328 | П | C | 515 | ш) | T | 3 | D | 520 | mla sa | 3 | M | ~1 | 525 | 0 | 310 | т1. |
| | _ | _ | туг | Tnr | ьeu | Asp | | H1S | rnr | arg | ттр | | туг | Cys | нта | тте |
| 331 | | 530 | ~ | | • | Τ. | 535 | | | | | 540 | *** | 77.2 | 77.2 | 77.5 |
| | _ | Thr | Cys | Ala | Asp | | Ala | Asp | Asp | Asp | | ьys | HlS | His | HlS | |
| | 545 | • | | | | 550 | | | | | 555 | | | | | 560 |
| | His | | | | _ | | | | | | | | | | | |
| 340 | <210 | J> SI | EQ II | ON C | : 5 | | | | | | | | | | | |

VERIFICATION SUMMARY

PATENT APPLICATION: US/09/600,991

DATE: 09/07/2001

TIME: 14:13:12

Input Set : A:\0471-0162P.ST25.txt

Output Set: N:\CRF3\09072001\I600991.raw

L:14 M:271 C: Current Filing Date differs, Replaced Current Filing Date